

200721009B

厚生労働科学研究費補助金

がん臨床研究事業

切除不能III期非小細胞肺癌に対する標準的治療の確立に関する研究

平成17年度～19年度 総合研究報告書

主任研究者 福岡 正博

平成20（2008）年 3月

平成 20 年 4 月 10 日

国立がんセンター総長 殿

住 所 〒631-0007 奈良県奈良市松陽台2-25-21  
フリカナ フカ マサヒロ  
研究者 氏 名 福岡 正博   
(所属機関 近畿大学医学部)

平成17年度から実施した厚生労働科学研究費補助金（がん臨床研究事業）に係る研究事業を完了したので、次のとおり報告する。

研究課題名（課題番号）：切除不能Ⅲ期非小細胞肺癌に対する標準的治療法の確立に関する研究(H17-がん臨床-一般-009)

国庫補助金精算所要額：金 58,045,000 円也  
(うち間接経費 0 円)

1. 厚生労働科学研究費補助金総合研究報告書表紙 (別添1のとおり)
2. 厚生労働科学研究費補助金総合研究報告書目次 (別添2のとおり)
3. 厚生労働科学研究費補助金総合研究報告書 (別添3のとおり)
4. 研究成果の刊行に関する一覧表 (別添4のとおり)
5. 研究成果による特許権等の知的財産権の出願・登録状況  
(総合研究報告書の中に書式に従って記入すること。)

---

別添 1

厚生労働科学研究費補助金総合研究報告書表紙

---

別添 2

厚生労働科学研究費補助金総合研究報告書目次

---

別添 3

厚生労働科学研究費補助金総合研究報告書

---

別添 4

研究成果の刊行に関する一覧表

厚生労働科学研究費補助金

がん臨床研究事業

切除不能III期非小細胞肺癌に対する標準的治療の確立に関する研究

平成17年度～19年度 総合研究報告書

主任研究者 福岡 正博

平成20（2008）年 3月

## 総合研究報告書目次

### 目 次

#### I. 総合研究報告

切除不能III期非小細胞肺癌に対する標準的治療の確立に関する研究

----- 1

福岡正博

#### II. 研究成果の刊行に関する一覧表

----- 10

#### III. 研究成果の刊行物・別刷

----- 24

厚生労働科学研究費補助金（がん臨床研究事業）  
（総合）研究報告書

切除不能III期非小細胞肺癌に対する標準的治療法の確立に関する研究班

主任研究者 福岡 正博 近畿大学医学部堺病院長

研究要旨切除不能限局型進行非小細胞肺癌の治療成績向上を目的とし、分子標的薬の上皮成長因子受容体（EGFR）チロシンキナーゼ阻害剤のゲフィチニブを組み込んだ新しい治療法についてその安全性を確認した上で有効性を検証する第Ⅲ相試験を実施することとした。対象を臨床病期Ⅲ期、70歳以下、未治療の非小細胞肺癌としたが、ゲフィチニブの有効な肺癌の臨床像、間質性肺障害（ILD）の危険因子を考慮してプロトコルを再三変更、腺癌で非喫煙ないし喫煙係数400以下あるいは10年以上禁煙している患者とした。治療方法は、シスプラチンとビノレルビンの併用化学療法を2サイクル投与後にゲフィチニブ250mgと胸部放射線照射2Gy1日1回、計60Gyを併用した。まず、Grade 2以上の肺臓炎を認めずに治療完遂できることを主要評価項目とした第Ⅰ/Ⅱ相試験を実施し、その認容性が確認できた後にランダム化第Ⅲ相試験を実施することとした。症例登録は平成16年10月から開始、平成20年2月28日までに32例が集積された。現時点では肺臓炎で中止した症例はなく、予測生存期間中央値は535日、2年生存率は49.5%で認容性のある治療法と思われるが、対象となる症例集団が少なく、第Ⅲ相試験は不可能と判断し、他の薬剤を用いた治療法の研究を行うこととした。

分担研究者氏名・所属機関名及び所属機関における職名

西條長宏（国立がんセンター東病院・副院長）、大江裕一郎（国立がんセンター中央病院・医長）、加藤治文（東京医科大学・教授）、西脇裕（国立がんセンター東病院・部長）、森清志（栃木県立がんセンター・医長）、岡本浩明（横浜市立市民病院・医長）、野田和正（神奈川県立がんセンター・部長）、横山晶（新潟県立がんセンター新潟病院・副院長）、樋田豊明（愛知県がんセンター・部長）、今村文生（大阪府立成人病センター・部長）、松井薫（大阪府立呼吸器・アレルギー医療センター・部長）、河原正明（独立行政法人近畿中央胸部疾患センター・診療部長）、西村恭昌（近畿大学医学部・教授）、根来俊一（兵庫県立成人病センター・部長）、早川和重（北里大学医学部・教授）、山本信之（静岡県立静岡がんセンター・部長）、中川和彦（近畿大学医学部・教授）

A. 研究目的

肺癌は我が国の悪性腫瘍死の第1位で年間62,000人以上が肺癌で死亡している。肺癌の70%以上は進行肺癌であり、その治療成績は極めて不良で5年生存率は15%程度である。近年、肺癌の中で約85%を占める非小細胞肺癌（NSCLC）に有効性が認められる分子標的薬として上皮成長因子受容体（EGFR）チロシンキナーゼ阻害剤（TKI）のゲフィチニブが開発された。本研究では、NSCLCの約30%を占める切除不能限局型Ⅲ期NSCLCの治療成績向上を目的とし、化学療法、胸部放射線治療（TRT）に分子標的薬のゲ

フィチニブを組み込んだ新しい治療法を考案し、その安全性と有効性を検討することとした。

B. 研究方法

ゲフィチニブは承認後に間質性肺障害（ILD）を発症することが明らかになり、また、ゲフィチニブと従来のプラチナ製剤を含む化学療法との併用では効果の増強が見られないことが明らかにされた。そこでまず、シスプラチンとビノレルビンの2剤併用化学療法後にゲフィチニブとTRTを併用する方法の認容性を検討し、これを試験治療として限局型局所進行NSCLCの標準治療とされているシスプラチン＋ビノレルビンとTRTを同時併用する治療法とのランダム化第Ⅲ相試験を実施することとした。対象は試験開始時には切除不能ⅢA/ⅢB期のNSCLCでPS 0, 1、20歳以上70歳以下としていたが、ゲフィチニブの有効性、ILD発症の危険因子を考慮して腺癌、非喫煙者ないし喫煙係数（1日の喫煙本数×喫煙年数）が400以下あるいは10年以上喫煙していない患者に限定した。治療法はシスプラチン80mg/m<sup>2</sup>をDay 1、ビノレルビン25mg/m<sup>2</sup>をDay 1, 8に投与し、これを3週間隔で2サイクル投与した後、2サイクル開始後 22日目よりゲフィチニブ250mg/dayを2週間投与し、胸部CTでILDの発現していないことを確認してからTRT 2 Gy、1日1回を週5日で6週間（総量 60Gy）照射することとした。TRTの照射範囲はV20 ≤ 35%または片肺の1/2を超えないとした。この試験の主要評価項目は、Grade 2以上の肺臓炎を認めず治療を完遂できた割合とし、その閾値を55%、期待値を90%で $\alpha=0.1$ 、 $\beta=0.2$ 、登録期間3年6ヶ月、追跡期間1年6ヶ月とした。その場合必要症例数は37例となる。

#### (倫理面への配慮)

本研究では、ゲフィチニブに起因するILDの発現を考慮し2剤併用化学療法を先行し、その後にゲフィチニブと放射線治療との併用を行うデザインとし、その安全性を十分検討した後にランダム化第Ⅲ相試験を開始するよう配慮した。また、適切な症例選択規準（腺癌、喫煙歴のない、または少ない患者など）、除外規準、治療中止規準を設け、個々の症例の安全性を確保するなど試験参加による不利益がないように努めた。ゲフィチニブによる早期の肺障害例を除外する目的でTRTとの併用開始前にゲフィチニブ単独投与時期を設定し、さらにTRT開始前に高分解能CT (HRCT) で肺障害のないことを確認するよう配慮した。さらに、ヘルシンキ宣言等の国際的倫理原則に従い、以下の事項を遵守することになっている。(1) 研究実施計画書 (プロトコル) をJCOGのプロトコル審査委員会の承認を得た後に各参加施設のIRB承認の得られた施設のみ症例登録を可能とする。(2) すべての患者に説明文書を用いて十分な説明を行い考慮の時間を設けた後に患者自身の自由意思による同意を本人より文書で取得する。(3) データの取り扱いに関して、直接個人を識別できる情報を用いず、個人情報保護を厳守する。(4) 本研究をJCOG試験とし臨床試験審査委員会、効果・安全性評価委員会、監査委員会を組織して研究の第3者の監視を行う。さらに、ゲフィチニブによる生存期間の延長は確認されていないなどの新しい情報を逐次患者に説明するよう配慮した。

#### C. 研究結果

本試験は平成16年10月より症例の登録を開始したが、先述の如くゲフィチニブの有効性と危険因子を考慮したプロトコルの改定を行ったため、実際に登録開始となったのは平成18年2月から平成20年3月13日現在35例の症例が登録された。現時点で32例の症例記録 (CRF) が回収されている。それらの症例の内訳は、男性11例、女性21例、年齢中央値60歳 (39~69歳)、PS 0が23例、1が9例、非喫煙者17例であった。Grade 2以上の肺臓炎は認めなかった。Grade 3, 4の好中球減少と貧血ともに4.5%、発熱性好中球減少症6.7%で他に重篤な血液毒性はなく、Grade 3, 4のGOT上昇が20%、GPT上昇が32%、悪心10%、嘔吐3.3%、食思不振13.3%などである。平成19年11月20日現在の推定生存期間中央値535日 (17.5ヵ月)、1年生存率90.4%、2年生存率49.5%である。

#### D. 考察

本研究においては、ゲフィチニブとTRTの併用により肺障害が高頻度に出現する可能性が危惧されたために極めて慎重な研究計画となった。肺臓炎は重喫煙者、扁平上皮癌、肺線維症などの既存の肺病変のある症例で多く発症し、また、ゲフィチニブが腺

癌、非喫煙者、女性、東洋人に有効性が高いことも示され、選択基準を厳しくし有効性が予測される患者に限定した。また、2<sup>nd</sup>-lineのNSCLCにおける、プラセボを対照とした無作為化比較試験 (ISEL試験) でゲフィチニブによる延命効果が見られなかったこと、腫瘍組織のEGFR遺伝子変異が有効性の予測に有用であることなどが示され、本研究の継続などに問題が提起された。しかし、東洋人の腺癌にEGFRの遺伝子変異例が多いこと、ISEL試験のサブセット解析において東洋人で有意な延命効果が見られたことから本試験を継続することとした。現時点では、本試験で治療された症例で重篤な肺毒性は出現していない。毒性としてはゲフィチニブによると思われるGrade 3, 4の肝障害が約3分の1の症例に認められているが完遂可能な治療法であり、現時点での推測生存期間、生存率は比較的良好と思われる。しかし、このような非喫煙者あるいは軽度喫煙歴の腺癌でⅢ期の症例はきわめて少なく、この治療法の有用性を確認するランダム化比較試験を実施することは困難であると判断し本研究は37例の集積で終了することとした。近年、EGFRのヒト化抗体やVEGFをターゲットとした薬剤 (抗体あるいはTKI)、新しい殺細胞抗がん剤などが開発されており、これらを組み入れた方法で新しい研究を開始することを考えている。

#### E. 結論

本研究に用いた併用化学療法後にゲフィチニブとTRTを併用する治療法は、現時点で重篤な肺障害は見られていない。シスプラチンとビノレルビンの併用化学療法後にゲフィチニブとTRTを併用する方法は実施可能な方法と思われる。しかし、非喫煙者 (あるいは軽度喫煙歴の患者)、腺癌のⅢ期で70歳以下の症例は極めて少なく、今回の症例集積からも標準治療を目指した第Ⅲ相試験を実施することは困難と考えた。したがって、切除不能限局型NSCLCの新しい治療法としては、他の分子標的薬、あるいは新しい殺細胞性抗がん剤を含めた治療法を考えるべきと結論した。

#### G. 研究発表

##### 1. 論文発表

1. Kudoh S., Nakamura S., Nakano T., Komuta K., Isobe T., Katakami N., Fukuda Y., Takada Y., Takada M., Fukuoka M., Ariyoshi Y.

Irinotecan and etoposide for previously untreated extensive-disease small cell lung cancer: A phase II trial of West Japan Thoracic Oncology Group.

Lung Cancer;49(2):263-269, 2005.

2. Matsui K., Hirashima T., Nitta T., Kobayashi M., Ogata Y., Furukawa M., Kudoh S., Yoshimura N., Mukohara T., Yamauchi S., Shiraishi S.,

Kamoi H., Negoro S., Takeda K., Nakagawa K., Takada M., Yana T., Fukuoka M.

A phase I/II study comparing regimen schedules of gemcitabine and docetaxel in Japanese patients with stage IIIB/IV non-small cell lung cancer.

Jpn J Clin Oncol. ;35(4):181-187, 2005.

3. Ohe Y., Negoro S., Matsui K., Nakagawa K., Sugiura T., Takada Y., Nishiwaki Y., Yokota S., Kawahara M., Saijo N., Fukuoka M., Ariyoshi Y.

Phase I-II study of amrubicin and cisplatin in previously untreated patients with extensive-stage small-cell lung cancer.

Ann Oncol. ;16(3):430-436, 2005.

4. Sugiura T., Ariyoshi Y., Negoro S., Nakamura S., Ikegami H., Takada M., Yana T., Fukuoka M.

Phase I/II study of amrubicin, a novel 9-amino anthracycline, in patients with advanced non-small-cell lung cancer.

Invest New Drugs;23(4):331-337, 2005.

5. Tamura K. and Fukuoka M.

Gefitinib in non-small cell lung cancer.

Expert Opin Pharmacother. ;6(6):985-993, 2005.

6. Bell DW., Lynch TJ., Haserlat SM., Harris P L., Okimoto R., Brannigan BW., Sgroi DC., Muir B., Riemenschneider MJ., Iacona RB., Krebs A D., Johnson DH., Giaccone G., Herbst RS., Manegold C., Fukuoka M., Kris MG., Baselga J., Ochs JS., Haber DA.

Epidermal growth factor receptor mutations and gene amplification in non-small-cell lung cancer: molecular analysis of the IDEAL/INTACT gefitinib trials.

J Clin Oncol. 1;23(31):8081-92, 2005.

7. Tsuboi M., Kato H., Nagai K., Tsuchiya R., Wada H., Tada H., Ichinose Y., Fukuoka M., Jiang H.

Gefitinib in the adjuvant setting: safety results from a phase III study in patients with completely resected non-small cell lung cancer.

Anticancer Drugs;16(10):1123-8, 2005.

8. Saito H., Takada Y., Ichinose Y., Eguchi K., Kudoh S., Matsui K., Nakagawa K., Takada M., Negoro S., Tamura K., Ando M., Tada T., Fukuoka M.

Phase II Study of Etoposide and Cisplatin With Concurrent Twice-Daily Thoracic Radiotherapy Followed by Irinotecan and Cisplatin in Patients With Limited-Disease Small-Cell Lung Cancer: West Japan Thoracic Oncology Group 9902.

J Clin Oncol. ;24(33):5247-52, 2006.

9. Ando M., Okamoto I., Yamamoto N., Takeda K., Tamura K., Seto T., Ariyoshi Y., Fukuoka M. Predictive factors for interstitial lung disease, antitumor response, and survival in non-small-cell lung cancer patients treated with gefitinib.

J Clin Oncol. ;24(16):2549-56, 2006.

10. Yamamoto N., Nakagawa K., Uejima H., Sugiura T., Takada Y., Negoro S., Matsui K., Kashii T., Takada M., Nakanishi Y., Kato T., Fukuoka M.

Randomized Phase II study of Carboplatin/Gemcitabine versus Vinorelbine/Gemcitabine in Patients With Advanced Non-small Cell Lung Cancer. West Japan Thoracic Oncology Group (WJTOG) 0104. Cancer 107, 599-605, 2006.

11. Kurata T., Tamura K., Okamoto I., Satoh T., Nakagawa K., Fukuoka M.

Pemetrexed-induced edema of the eyelid.

Lung Cancer 54, 241-242, 2006.

12. Nakagawa K., Kudoh S., Matsui K., Negoro S., Yamamoto N., Latz J. E., Adachi S., Fukuoka M.

A phase I study of pemetrexed (LY231514) supplemented with folate and vitamin B12 in Japanese patients with solid tumours.

Br. J. Cancer 95, 677-682, 2006.

13. Kurata T., Matsuo K., Takada M., Kawahara M., Tsuji M., Matsubara Y., Otani N., Matsuyama S., Muraishi K., Fujita T., Ishikawa M., Koyano K., Okamoto I., Satoh T., Tamura K., Nakagawa K., Fukuoka M.

Is the Importance of Achieving Stable Disease Different between Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors and Cytotoxic Agents in the Second-Line Setting for Advanced Non-small Cell Lung Cancer?

Journal of Thoracic Oncology 1 684-691, 2006.

14. Yoshimura N., Kudoh S., Kimura T., Mitsuoka S., Matsuura K., Hirata K., Matsui K., Negoro S., Nakagawa K., Fukuoka M.

EKB-569, a new irreversible epidermal growth factor receptor tyrosine kinase inhibitor, with clinical activity in patients with non-small cell lung cancer with acquired resistance to gefitinib.

Lung Cancer 51:363-368, 2006.

15. Kudoh S, Takeda K, Nakagawa K, Takada M, Kakutani N, Matsui K, Shinkai T, Sawa T, Goto I, Semba H, Seto T, Ando M, Satoh T, Yoshimura N, Negoro S, Fukuoka M.

Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904).

J Clin Oncol 24: 3657-3663, 2006.

16. Yonesaka K., Tamura K., Kurata T., Satoh T., Ikeda M., Fukuoka M., Nakagawa K. Small interfering RNA targeting survivin sensitizes lung cancer cell with mutant p53 to adriamycin.

Int J Cancer 118: 812-820, 2006.

17. Yamamoto N., Tsurutani J., Yoshimura N., Asai G., Moriyama A., Nakagawa K., Kudoh S., Takada M., Minato Y., Fukuoka M.

Phase II study of weekly paclitaxel for Relapsed and refractory small cell lung cancer.

Anticancer Res 26: 777-781, 2006.

18. Okamoto I., Araki J., Suto R., Shimada M., Nakagawa K., Fukuoka M.

EGFR mutation in gefitinib-responsive small-cell lung cancer.

Ann Oncol 17:1028-1029, 2006.

19. Asai G., Yamamoto N., Kurata T., Tamura K., Uejima H., Nakagawa K., Fukuoka M.

Phase I and Pharmacokinetic Study of Combination Chemotherapy Using Irinotecan and paclitaxel in Patients with Lung Cancer.

J Thorac Oncol. (1) : 226-230, 2006.

20. Kaneda H., Kurata T., Tamura K., Uejima H., Nakagawa K., Fukuoka M.

A Phase I Study of Irinotecan in Combination with Amrubicin for Advanced Lung Cancer Patients.

Anticancer Res. 26: 2479-2486, 2006.

21. Yamamoto N., Nishimura Y., Nakagawa K., Mat

sui K., Fukuoka M.

Phase I/II study of weekly docetaxel dose escalation in combination with fixed weekly cisplatin and concurrent thoracic radiotherapy in locally advanced non-small cell lung cancer.

Cancer Chemother Pharmacol. 58(3):285-291, 2006.

22. Kris MG., Giaccone G., Davies A., Fukuoka M., Garfield DH., Jassem J., Quoix EA., Sandler AB., Scagliotti GV., Van Meerbeek JP., West H.

Systemic therapy of bronchioloalveolar carcinoma: results of the first IASLC/ASCO consensus conference on bronchioloalveolar carcinoma.

J Thorac Oncol. 1(9 Suppl):S32-6, 2006

23. Ohe Y., Ohashi Y., Kubota K., Tamura T., Nakagawa K., Negoro S., Nishiwaki Y., Saijo N., Ariyoshi Y., Fukuoka M.

Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small-cell lung cancer: Four-Arm Cooperative Study in Japan. Ann. Oncol. 18(2):317-23, 2007.

24. Akashi Y., Okamoto I., Suzuki M., Tamura K., Iwasa T., Hisada S., Satoh T., Nakagawa K., Ono K., Fukuoka M.

The novel microtubule-interfering agent TZT-1027 enhances the anticancer effect of radiation in vitro and in vivo.

Br J Cancer. 96(10):1532-9, 2007.

25. Tsuya A., Kurata T., Tamura K., Fukuoka M. Skeletal metastases in non-small cell lung cancer: A retrospective study.

Lung Cancer. 57(2):229-32, 2007.

26. Takeda K., Takifuji N., Negoro S., Furuse K., Nakamura S., Takada Y., Hosono T., Hayasaka S., Nakano T., Araki J., Senba H., Iwami F., Yamaji Y., Fukuoka M., Ikegami H.

Phase II study of amrubicin, 9-amino-anthracycline, in patients with advanced non-small-cell lung cancer: a West Japan Thoracic Oncology Group study.

Invest New Drugs. 25(4):377-83, 2007.

27. Okabe T., Okamoto I., Tamura K., Terashima M., Yoshida T., Satoh T., Takada ., Fukuoka M., Nakagawa K.

Differential constitutive activation of the ep

idermal growth factor receptor in non-small cell lung cancer cells bearing EGFR gene mutation and amplification.

Cancer Res. 67(5):2046-53, 2007.

28. Tamura K., Nakagawa K., Kurata T., Satoh T., Nogami T., Takeda K., Mitsuoka S., Yoshimura N., Kudoh S., Negoro S., Fukuoka M.

Phase I study of TZT-1027, a novel synthetic diolastatin 10 derivative and inhibitor of tubulin polymerization, which was administered to patients with advanced solid tumors on days 1 and 8 in 3-week courses.

Cancer Chemother Pharmacol. 60(2):285-93, 2007.

29. Yana T., Negoro S., Takada M., Yokota S., Takada Y., Sugiura T., Yamamoto H., Sawa T., Kawahara M., Katakami N., Ariyoshi Y., Fukuoka M.

Phase II study of amrubicin in previously untreated patients with extensive-disease small cell lung cancer: West Japan Thoracic Oncology Group study.

Invest New Drugs. 25(3):253-8, 2007.

30. Ikeda M., Okamoto I., Tamura K., Satoh T., Yonesaka K., Fukuoka M., Nakagawa K.

Down-regulation of survivin by ultraviolet C radiation is dependent on p53 and results in G(2)-M arrest in A549 cells.

Cancer Lett. 248(2):292-8, 2007.

31. Nishimura Y., Nakagawa K., Takeda K., Tanaka M., Segawa Y., Tsujino K., Negoro S., Fuwa N., Hida T., Kawahara M., Katakami N., Hirokawa K., Yamamoto N., Fukuoka M., Ariyoshi Y.

Phase I/II Trial of Sequential Chemoradiotherapy Using a Novel Hypoxic Cell Radiosensitizer, Doranidazole (Pr-350), in Patients with Locally Advanced Non-Small-Cell Lung Cancer (Wjtog-0002).

Int J Radiat Oncol Biol Phys. 69(3):786-92, 2007.

32. Kurata T., Okamoto I., Tamura K., Fukuoka M.

Amrubicin for non-small-cell lung cancer and small-cell lung cancer.

Invest New Drugs. 2007 Oct;25(5):499-504, 2007.

33. Morinaga R., Okamoto I., Furuta K., Kawano Y., Sekijima M., Dote K., Satou T., Nishio K., Fukuoka M., Nakagawa K.

Sequential occurrence of non-small cell and small cell lung cancer with the same EGFR mutation.

Lung Cancer. 58(3):411-3, 2007

34. Shimizu T., Satoh T., Tamura K., Ozaki T., Okamoto I., Fukuoka M., Nakagawa K.

Oxaliplatin/fluorouracil/leucovorin (FOLFOX4 and modified FOLFOX6) in patients with refractory or advanced colorectal cancer: post-appraisal Japanese population experience.

Int J Clin Oncol. 12(3):218-23, 2007

35. Yoshida K., Sugiura T., Takifuji N., Kawahara M., Matsui K., Kudoh S., Takada M., Fukuoka M., Ariyoshi Y., Fukuda H., Saijo N.

Randomized phase II trial of three intrapleural therapy regimens for the management of malignant pleural effusion in previously untreated non-small cell lung cancer: JCOG 9515.

Lung Cancer. 58(3):362-8, 2007.

36. Ozaki T., Tamura K., Satoh T., Kurata T., Shimizu T., Miyazaki M., Okamoto I., Nakagawa K., Fukuoka M.

Phase I study of combination therapy with S-1 and weekly docetaxel for advanced gastric cancer.

Anticancer Res. 27(4C):2657-65, 2007.

37. Marko-Varga G., Ogiwara A., Nishimura T., Kawamura T., Fujii K., Kawakami T., Kyono Y., Tu HK., Anyoji H., Kanazawa M., Akimoto S., Hirano T., Tsuboi M., Nishio K., Hada S., Jiang H., Fukuoka M., Nakata K., Nishiwaki Y., Kunito H., Peers IS., Harbron CG., South MC., Higenbottam T., Nyberg F., Kudoh S., Kato H.

Personalized medicine and proteomics: lessons from non-small cell lung cancer.

J Proteome Res. 6(8):2925-35, 2007.

38. Yoshida T., Okamoto I., Okabe T., Iwasa T., Satoh T., Nishio K., Fukuoka M., Nakagawa K.

Matuzumab and cetuximab activate the epidermal growth factor receptor but fail to trigger downstream signaling by Akt or Erk.

Int J Cancer. 122(7):1530-8, 2008.

39. Akashi Y., Okamoto I., Iwasa T., Yoshida T., Suzuki M., Hatashita E., Yamada Y., Satoh T., Fukuoka M., Ono K., Nakagawa K.

Enhancement of the antitumor activity of ionizing radiation by nimotuzumab, a humanised monoclonal antibody to the epidermal growth factor receptor, in non-small cell lung cancer cell lines of differing epidermal growth factor receptor status. *Br J Cancer*. 2008

## 2. 学会発表

### 1. M. Fukuoka

“IRESSA – A new standard in second line”  
Asia Pacific Oncology Summit meeting & Scientific Seminar on target Therapy & EGFR, Seoul, Korea. 2005.

### 2. T. Satoh, K. Tamura, K. Nakagawa, T. Kurata, T. Nogami, M. Fukuoka.

S-1 plus docetaxel in patients with metastatic gastric cancer: A phase I study.  
Gastrointestinal Cancers Symposium, Miami, U.S.A. 2005.

### 3. K. Matsui, S. Negoro, S. Kudoh, K. Nakagawa, T. Hirashima, K. Takeda, N. Yoshimura, M. Fukuoka.

EKB-569: An irreversible EGFR tyrosine kinase inhibitor.  
11th World Conference on Lung Cancer, Barcelona, Spain, 2005.

### 4. K. Nakagawa, S. Kudoh, K. Matsui, N. Yamamoto, J. Latz, S. Adachi, M. Fukuoka.

A Phase I Study of Pemetrexed Supplemented with Folic acid (FA) and Vitamin B12 (VB12) in Japanese Patients with Solid Tumors.  
11th World Conference on Lung Cancer, Barcelona, Spain, 2005.

### 5. Masato. Ikeda, Kenji. Tamura, Kimio. Yonesaka, Taroh. Satoh, Takayasu. Kurata, Toshiji. Nogami, Kazuhiko. Nakagawa, and, Masahiro. Fukuoka.

Small interfering RNA targeting survivin sensitizes lung cancer cell with mutant p53 to ionizing radiation.  
96th American Association for Cancer Research Annual Meeting, Anaheim, U.S.A. 2005.

### 6. Yataro. Daigo, Nobuhisa. Ishikawa, Soji. Kakiuchi, Tatsuhiro. Tsunoda, Seiji. Yano, Kazuhiko. Nakagawa, Takashi. Tsuruo, Nobuoki. Kohno, Masahiro. Fukuoka, Saburo. Sone, and, Yusuke. Nakamura.

Prediction of sensitivity of advanced non-small cell lung cancers to gefitinib (Iressa ZD1839) and its application to the development of

diagnostic test.

96th American Association for Cancer Research Annual Meeting, Anaheim, U.S.A. 2005.

### 7. T. J. Lynch, D. Bell, D. Haber, D. Johnson, G. Giaccone, M. Fukuoka, M. Kris, R. Herbst, A. Krebs, J. Ochs.

Correlation of molecular markers including mutations with clinical outcomes in advanced non-small cell lung cancer (NSCLC) patients (pts) treated with gefitinib, chemotherapy or chemotherapy and gefitinib in IDEAL and INTACT clinical trials.

41st American Society of Clinical Oncology Annual Meeting, Orlando, U.S.A. 2005.

### 8. H. Saka, N. Nogomi, S. Kitaguti, M. Yamamoto, M. Fukuoka, Y. Ariyoshi; West Japan Thoracic Oncology Group, Osaka, Japan.

Phase I/II trial of carboplatin (CBDCA)/ weekly paclitaxel in patients with advanced non-small cell lung cancer in Japanese population: WJTOG 9907.

41st American Society of Clinical Oncology Annual Meeting, Orlando, U.S.A. 2005.

### 9. K. Tamura, I. Okamoto, T. Kurata, T. Satoh, K. Nakagawa, M. Fukuoka.

Low expressions of surfactant-associated protein (SP-A) in cancer tissues or in normal bronchial epithelial cells by immuno-histochemistry predict interstitial lung diseases (ILDs) induced by gefitinib in patients with advanced non-small cell lung cancer (NSCLC).

41st American Society of Clinical Oncology Annual Meeting, Orlando, U.S.A. 2005.

### 10. K. Nakagawa, M. Fukuoka, N. Saijo.

Weekly Paclitaxel (P) in patients with advanced Non-Small Cell Lung Cancer.

41st American Society of Clinical Oncology Annual Meeting, Orlando, U.S.A. 2005.

### 11. K. Takeda, S. Kudoh, K. Nakagawa, M. Takada, N. Katakami, K. Matsui, M. Andoh, T. Satoh, S. Negoro, M. Fukuoka.

Randomized phase III study of docetaxel (D) versus vinorelbine (V) for elderly patients (pts) with advanced non-small cell lung cancer (NSCLC): Results of a West Japan Thoracic Oncology Group trial (WJTOG9904).

41st American Society of Clinical Oncology Ann

ual Meeting, Orlando, U. S. A. 2005.

12. T. Kurata, H. Kaneda, K. Tamura, T. Satoh, T. Nogami, H. Uejima, K. Nakagawa, M. Fukuoka.

A combination phase I study of Amrubicin and Irinotecan (CPT-11) in patients with lung cancer.

41th American Society of Clinical Oncology Annual Meeting, Orlando, U. S. A. 2005.

13. Terashima. Masaaki, Isamu. Okamoto, Kenji. Tamura, Takafumi. Okabe, Taro. Sato, Minoru. Takada, Kazuhiko. Nakagawa, and, Masahiro. Fukuoka.

Relationship between EGFR protein expression EGFR gene amplification EGFR gene mutations and gefitinib sensitivity in human non-small cell lung cancer cell lines.

97th American Association for Cancer Research Annual Meeting, Washington D. C. , U. S. A. 2006.

14. Yusakuk. Akashi, Taroh. Satoh, Isamu. Okamoto, Kenji. Tamura, Masaaki. Terashima, Takafumi. Okabe, Minoru. Suzuki, Koji. Ono, Kazuhiko. Nakagawa, and, Masahiro, Fukuoka.

Cell cycle regulation and radiosensitization of TZT-1027 a novel antimicrotubule agent.

97th American Association for Cancer Research Annual Meeting, Washington D. C. , U. S. A. 2006.

15. T. Kurata, H. Saito, K. Nakagawa, T. Kashii, K. Take da, Y. Iwamoto, N. Iwamoto, N. Katakami, T. Nakamo, M. Fukuoka.

Randomized phase II study of carboplatin and paclitaxel (CP) versus gemcitabine and vinorelbine (GV) in performance status (PS) 2 patients with advanced non-small cell lung cancer (NSCLC) : preliminary results of west Japan thoracic oncology group 0004.

31th Congress of the European Society for Medical Oncology, Istanbul, Turkey. 2006.

16. K. Tamura, Y. Nisiwaki, T. Tamura, K. Nakagawa, K. Matsui, K. Watanabe, N. Saijo, M. Fukuoka.

A phase II study of the HER1/EGFR tyrosine kinase inhibitor (TKI) erlotinib Japanese patients with non-small cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy.

31th Congress of the European Society for Medical Oncology, Istanbul, Turkey. 2006.

17. T. Satoh, K. Tamura, I. Okamoto, M. Miyazak, T. Shim

izu, T. Ozaki, K. Nakagawa, M. Fukuoka.

S-1 plus docetaxel in patients with advanced gastric cancer: A phase I study.

Gastrointestinal Cancers Symposium, San Francisco, U. S. A. 2006.

18. H. Kaneda, K. Nakagawa, H. Saito, T. Kashii, Y. Iwamoto, N. Katakami, T. Nakano, T. Kurata, M. Fukuoka.

Randomized phase II study of carboplatin and paclitaxel (CP) versus gemcitabine and vinorelbine (GV) in performance status (PS) 2 patients with advanced non-small cell lung cancer (NSCLC): Preliminary results of West

Japan Thoracic Oncology Group 0004.

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

19. K. Takeda, S. Negoro, K. Nakagawa, Y. Segawa, Y. Nishimura, M. Fukuoka, Y. Ariyoshi.

Phase I/II trial of doranidazole (PR-350) and concurrent thoracic radiotherapy (TRT) in patients (pts) with locally advanced (LA) non-small cell lung cancer (NSCLC).

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

20. K. Nakagawa, K. Kiura, T. Shinkai, K. Eguchi, Y. Ohe, N. Yamamoto, M. Tsuboi, S. Yokota, M. Fukuoka, H. Jiang.

A randomized double-blind phase IIa dose-finding study of ZD6474 in Japanese patients with NSCLC.

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

21. T. Ozaki, T. Satoh, T. Shimizu, M. Miyazaki, T. Kurata, M. Fukuoka, K. Tamura.

A phase I study of combination S-1 and weekly docetaxel (TXT) for advanced or recurrent gastric cancer.

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

22. I. Okamoto, T. Kashii, Y. Urata, T. Hirashima, S. Kudoh, Y. Ichinose, N. Ebi, T. Satoh, K. Tamura, M. Fukuoka.

EGFR mutation-based phase II multicenter trial of gefitinib in advanced non-small cell lung cancer (NSCLC) patients (pts): Results of West Japan Thoracic Oncology Group trial (WJTOG0403).

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

23. K. Goto, Y. Nishiwaki, N. Saijo, K. Takeda, N. Katakami, S. Kudoh, Y. Ichinose, Y. Ohashi, Y. Ariyoshi, M. Fukuoka.

The Four-Arm Cooperative Study (FACS) for advanced non-small cell lung cancer (NSCLC): A subgroup analysis in elderly patients (pts).

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

24. Y. Yamada, T. Shimizu, T. Ozaki, E. Hatashita, T. Kurata, M. Fukuoka, K. Tamura.

Rapid detection of UGT1A1 polymorphisms by a novel microarray assay: A radiation study using 100 samples from patients with lung cancer treated by irinotecan.

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

25. T. Shimizu, Y. Yamada, K. Shirao, H. Yasui, H. Morita, K. Tamura, T. Ozaki, M. Fukuoka.

Clinical application of immunoreactivity of dihydropyrimidine dehydrogenase (DPD) using highly specific antibody against recombinant human DPD (rhDPD) in gastric scirrhous cancer treated with S-1, new DPD inhibitory fluropyrimidine.

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

26. K. Tamura, I. Okamoto, T. Ozaki, T. Shimizu, T. Kashii, K. Takeda, K. Matsui, S. Kudoh, T. Kurata, M. Fukuoka.

A phase I dose-escalating study of combination S-1 and carboplatin (CBDCA) in patients with chemo-naïve advanced non-small cell lung cancer (NSCLC).

42th American Society of Clinical Oncology Annual Meeting, Atlanta, U. S. A. 2006.

27. K. Nakagawa, T. Satoh, I. Okamoto, M. Miyazaki, R. Morinaga, A. Tsuya, Y. Hasegawa, M. Terashima, S. Ueda, M. Fukuoka.

Phase I study of YM155, a first-in-class survivin suppressant, in patients with advanced solid tumors in Japan.

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

28. S. Niho, Y. Ichinose, T. Tamura, N. Yamamoto, M. Tsuboi, K. Nakagawa, T. Shinkai, H. Jiang, Y. Nishiwaki, M. Fukuoka.

Results of a randomized phase III study to compare the overall survival of gefitinib versus docetaxel in Japanese patients with non-small cell lung cancer who failed one or two chemotherapy regimens.

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

29. Y. Ichinose, K. Nakagawa, T. Tamura, K. Kubota, N. Yamamoto, S. Adachi, Y. Nambu, Y. Nishiwaki, N. Saijo, M. Fukuoka.

A randomized phase II study of 500 mg/m<sup>2</sup> and 1,000 mg/m<sup>2</sup> of pemetrexide patients (pts) with locally advanced or metastatic non-small cell lung cancer (NSCLC) who had prior chemotherapy.

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

30. T. Hirashima, K. Nakagawa, T. Kashii, A. Kubo, J. Sasakai, K. Tanaka, S. Sato, T. Kurata, K. Tamura, M. Fukuoka.

Correlative study of EGFR mutations or protein expressions of EGFR, phosphorylated EGFR, HER2, phosphorylated HER2 and IGF-1 with gefitinib sensitivity in patients with non-small cell lung cancer: Results of West Japan Thoracic Oncology Group trial (WJTO).

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

31. Y. Iwamoto, H. Saito, K. Nakagawa, T. Kashii, N. Katakami, T. Nakano, T. Kurata, M. Ando, M. Fukuoka.

A randomized phase II study of carboplatin and paclitaxel (CP) versus gemcitabine and vinorelbine (GV) in performance status (PS) 2 patients with advanced non-small cell lung cancer (NSCLC): West Japan Thoracic Oncology Group 00.

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

32. T. Kashii, T. Kurata, K. Takeda, N. Seki, M. Tsuboi, T. Miwa, R. Morinaga, M. Kobayashi, T. Satoh, M. Fukuoka.

A combination phase I study of topotecan with carboplatin for relapsed small cell lung cancer: Results of West Japan Thoracic Oncology Group trial (WJTOG0202).

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

33. K. Gemba, K. Yamazaki, H. Kunitoh, T. Hida, K. Nakagawa, T. Shinkai, Y. Ichinose, Y. Nambu, N. Sij

o, M. Fukuoka.

A phase I/II study of pemetrexed plus cisplatin in Japanese patients with malignant pleural mesothelioma.

43th American Society of Clinical Oncology Annual Meeting, Chicago, U. S. A. 2007.

H. 知的財産権の出願・登録状況

1. 特許取得

なし

2. 実用新案登録

なし  
3. その他  
なし

## 雑誌

Matsui, K., Hirashima, T., Nitta, T., Kobayashi, M., Ogata, Y., Furukawa, M., Kudoh, S., Yoshimura, N., Mukohara, T., Yamauchi, S., Shiraishi, S., Kamoi, H., Negoro, S., Takeda, K., Nakagawa, K., Takada, M., Yana, T., Fukuoka, M.	A phase I/II study comparing regimen schedules of gemcitabine and docetaxel in Japanese patients with stage IIIB/IV non-small cell lung cancer.	Jpn J Clin Oncol.	35(4)	181-187	2005
Mori K, Kamiyama Y, Kondo T, Kano Y, Kodama T	A phase II study of docetaxel and infusional cisplatin in advanced non-small-cell lung cancer	Chemotherapy	51(2-3)	120-5	2005
Ishikura S, Ohe Y, Nihei K, Kubota K, Kakinuma R, Ohmatsu H, Goto K, Niho S, Nishiwaki Y, Ogino T.	A phase II study of hyperfractionated (HART) after induction cisplatin (CDDP) and vinorelbine (VNR) for stage III non-small-cell lung cancer (NSCLC).	Int J Radiat Oncol Biol Phys	61	1117-1122	2005
Ohe Y	Chemoradiotherapy for lung cancer	Expert Opin Pharmacother	6	2793-2804	2005
Yamazaki S, Sekine I, Matsuno Y, Takei H, Yamamoto N, Kunitoh H, Ohe Y, Tamura T, Kodama T, Asamura H, Tsuchiya R, Saijo N.	Clinical responses of large cell neuroendocrine carcinoma of the lung to cisplatin-based chemotherapy.	Lung Cancer	49	217-223	2005
Fujii K, Nakano T, Kato H, et al.	Clinical-scale high-throughput human plasma proteome analysis: Lung adenocarcinoma.	Proteomics	5	1150-1159	2005
Mori K, Niki N, Kondo T, Kamiyama Y, Kodama T, Kawada Y, Moriyama N	Development of a novel computer-aided diagnosis system for automatic discrimination of malignant from benign solitary pulmonary nodules on thin-section dynamic computed tomography	J Comput Assist Tomogr	29(2)	215-22	2005
Sasaki.H.,Endo.K.,Konishi.A.,Takada.M.,Kawahara.M.,Iuchi.K.,Matsumura.A.,Okumura.M.,Tanaka.H.,Kawaguchi.T.,Shimizu.T.,Takeuchi.H.,Yano.M.,Fukai.I.,and Fujii.Y	EGFR Mutation Status in Japanese Lung Cancer Patients: Genotyping Analysis Using LightCycler.	Clin Cancer Res	11	2924-2929	2005
大原房子、高野利実、大江裕一郎	EGFR阻害剤と他の分子標的薬との併用療法.	分子呼吸器病	9	168-171	2005
Ando K, Ohmori T, Inoue F, Kadofuku T, Hosaka T, Ishida H, Shirai T, Okuda K, Hirose T, Horichi N, Nishio K, Saijo N, Adachi M, Kuroki T.	Enhancement of sensitivity to tumor necrosis factor alpha in non-small cell lung cancer cells with acquired resistance to gefitinib.	Clin Cancer Res	11(24 Pt 1)	8872-8879	2005
Endo.K.,Konishi.A.,Sasaki.H.,Takada.M.,Tanaka.H.,Okumura.M.,Kawahara.M.,Sugiura.H.,Kuwabara.Y.,Fukai.I.,Matsumura.A.,Yano.M.,Kobayashi.Y.,Mizuno.K.,Haseda.H.,Suzuki.E.,Iuchi.K.,Fujii.Y	Epidermal growth factor receptor gene mutation in non-small cell lung cancer using highly sensitive and fast TaqMan PCR assay	Lung Cancer	50	375-384	2005
Takano T, Ohe Y, Sakamoto H, Tsuta K, Matsuno Y, Tateishi U, Yamamoto S, Nokihara H, Yamamoto N, Sekine I, Kunitoh H, Shibata T, Sakiyama T, Yoshida T, Tamura T	Epidermal Growth Factor Receptor Gene Mutations and Increased Copy Numbers Predict Gefitinib Sensitivity in Patients with Recurrent Non-Small-Cell Lung Cancer.	J Clin Oncol	23	6829-6837	2005

Bell DW, Lynch TJ, Haserlat SM, Harris PL, Okimoto RA, Brannigan BW, Sgroi DC, Muir B, Riemenschneider MJ, Iacona RB, Krebs AD, Johnson DH, Giaccone G, Herbst RS, Manegold C, <u>Fukuoka M</u> , Kris MG, Baselga J, Ochs JS, Haber DA.	Epidermal growth factor receptor mutations and gene amplification in non-small-cell lung cancer: molecular analysis of the IDEAL/INTACT gefitinib trials.	J Clin Oncol.	1;23(31)	8081-92	2005
Takano T, <u>Ohe Y</u>	Erlotinib in lung cancer	N Engl J Med	353	1739-1741	2005
Koizumi F, Shimoyama T, Taguchi F, <u>Saijo N</u> , Nishio K.	Establishment of a human non-small cell lung cancer cell line resistant to gefitinib.	Int J Cancer	116	36-44	2005
Nakamura H, Fujita K, <u>Kato H</u> , et al.	Expression pattern of the scaffold protein IQGAP1 in lung cancer.	Oncology Report	13(3)	427-431	2005
Kato Y, Hirano T, <u>Kato H</u> , et al.	Frequent loss of E-cadherin and/or catenins in intrabronchial lesions during carcinogenesis of the bronchial epithelium.	Lung Cancer	48(3)	323-330	2005
Tsuboi M, <u>Kato H</u> , Nagai K, Tsuchiya R, Wada H, Tada H, Ichinose Y, <u>Fukuoka M</u> , Jiang H.	Gefitinib in the adjuvant setting: safety results from a phase III study in patients with completely resected non-small cell lung cancer.	Anticancer Drugs.	16(10)	1123-8	2005
Oshita F, Ikehara M, Sekiyama A, Hamanaka N, Saito H, Yamada K, <u>Noda K</u> , Kameda Y, Miyagi Y.	Genomicwide cDNA microassay screening of genes related to benefits and toxicities platinum-based chemotherapy in patients with advanced lung cancer.	Am J Clin Oncol	28(4)	367-370	2005
Tamura, K. and <u>Fukuoka, M.</u>	Gefitinib in non-small cell lung cancer.	Expert Opin Pharmacother	6(6)	985-993	2005
<u>Nishimura Y</u> , Nakamatsu K, Shibata T, Kanamori S, Koike R, Okumura M, Suzuki M.	Importance of the initial volume of parotid glands in xerostomia for patients with head and neck cancers treated with IMRT.	Jpn J Clin Oncol	35	375-9	2005
Kudoh, S., Nakamura, S., Nakano, T., Komuta, K., Isobe, T., Katakami, N., Fukuda, Y., Takada, Y., Takada, M., <u>Fukuoka, M.</u> , Ariyoshi, Y.	Irinotecan and etoposide for previously untreated extensive-disease small cell lung cancer: A phase II trial of West Japan Thoracic Oncology Group.	Lung Cancer	49(2)	263-269	2005
<u>Saijo N.</u>	Is radiotherapy optimally combined with chemotherapy in elderly patients with limited-stage small-cell lung cancer?	Nat Clin Pract Oncol	2(11)	550-551	2005
Furukawa K, <u>Kato H</u> , Ebihara Y, et al.	Locally Recurrent Central- Type Early Stage Lung Cancer < 1.0 cm in Diameter After Complete Remission by Photodynamic Therapy.	CHEST	128(5)	3269-3275	2005
Furukawa K, Miura T, <u>Kato H</u> , et al	Microwave coagulation Therapy in Canine Peripheral Lung Tissue.	J. of Surgical Research	123	245-250	2005
Mitsudomi, T., Kosaka, T., Endoh, H., Horio, Y., <u>Hida, T.</u> , Mori, S., Hatooka, S., Shinoda, M., Takahashi, T., and Yatabe, Y.	Mutations of the epidermal growth factor receptor gene predict prolonged survival after gefitinib treatment in patients with non-small cell lung cancer with postoperative recurrence.	J Clin Oncol.	23	2513-20	2005
<u>Ohe Y.</u> , <u>Negoro S.</u> , <u>Matsui K.</u> , <u>Nakagawa K.</u> , <u>Sugiura T.</u> , <u>Takada Y.</u> , <u>Nishiwaki Y.</u> , <u>Yokota S.</u> , <u>Kawahara M.</u> , <u>Saijo N.</u> , <u>Fukuoka M.</u> , & <u>Ariyoshi Y.</u> On behalf of the Amrubicin SCLC Study Group.	Phase I - II study of amrubicin and cisplatin in previously untreated patients with extensive-stage small-cell lung cancer	Ann Oncol	16(3)	430-6	2005

Sugiura, T., Ariyoshi, Y., <u>Negoro, S.</u> , Nakamura, S., Ikegami, H., Takada, M., Yana, T., <u>Fukuoka, M.</u>	Phase I/II study of amrubicin, a novel 9-aminoanthracycline, in patients with advanced non-small-cell lung cancer.	Invest New Drugs	23(4)	331-337	2005
Tsuchiya R, Suzuki K, <u>Kato H.</u> et al.	Phase II trial of postoperative adjuvant cisplatin and etoposide in patients with completely resected stage I-IIIa small cell lung cancer. The Japan Clinical Oncology Lung Cancer Study Group Trial (JCOG9101).	J of Thoracic and Cardiovascular Surgery	129(5)	977-983	2005
Kubota K, <u>Nishiwaki Y.</u> , Sugiura T, <u>Noda K.</u> , <u>Mori K.</u> , <u>Kawahara M.</u> , <u>Negoro S.</u> , Watanabe K, Imamura F, Tamura T, <u>Saijo N.</u>	Pilot study of concurrent etoposide and cisplatin plus accelerated hyperfractionated thoracic radiotherapy followed by irinotecan and cisplatin for limited-stage small cell lung cancer. Japan Clinical Oncology Group 9903.	Clin Cancer Res	11(15)	5634-5638	2005
Takamochi K, Yoshida J, Murakami K, Niho S, Ishii G, Nishimura M, <u>Nishiwaki Y.</u> , Suzuki K, Nagai K.	Pitfalls in lymph node staging with positron emission tomography in non-small cell lung cancer patients.	Lung Cancer , 2005.	47	235-242	2005
<u>Kato H.</u> , Tsuboi M, Kato Y, et al.	Postoperative adjuvant therapy for completely resected early-stage non-small cell lung cancer.	Int. J Clinical Oncology	10	157-164,	2005
Nakamura H, Aute I, Kawasaki N, Taguchi M, Ohira T, <u>Kato H</u>	Quantitative Detection of Lung Cancer Cells by Fluorescence in Situ Hybridization - Comparison With Conventional Cytology.	CHEST	128(2)	906-911	2005
<u>Yamamoto N.</u> , Tamura T, Murakami H, Shimoyama T, Nokihara H, Ueda Y, Sekine I, Kunitoh H, <u>Ohe Y.</u> , Kodama T, Shimizu M, Nishio K, Ishizuka N, <u>Saijo N.</u>	Randomized pharmacokinetic and pharmacodynamic study of docetaxel: dosing based on body-surface area compared with individualized dosing based on cytochrome P450 activity estimated using a urinary metabolite of exogenous cortisol.	J Clin Oncol	23(6)	1061-1069	2005
Matsuguma H, Nakahara R, Kondo T, Kamiyama Y, <u>Mori K.</u> , Yokoi K	Risk of pleural recurrence after needle biopsy in patients with resected early stage lung cancer.	Ann Thorac Surg	80(6)	2026-31	2005
Hiromichi Ishiyama, Masashi Kitano, Yuzuru Niibe, Mineko Uemae, <u>Kazushige Hayakawa</u>	Simple technique to visualize random set-up displacements using a commercially available radiotherapy planning system.	Radiat Med	23(3)	216- 219	2005
Yonesaka,K, Tamura,K, Kurata,T., Satoh,T., Ikeda,M., <u>Fukuoka,M.</u> , <u>Nakagawa,K.</u>	Small interfering RNA targeting survivin sensitizes lung cancer cell with mutant p53 to adriamycin.	Int J Cancer	118	812-820	2005
Atagi S, Kawahara M, Tamura T, <u>Noda K.</u> , <u>Watanabe K.</u> , <u>Yokoyama A.</u> , Sugiura T, Senba H, Ishikura S, Ikeda H, Ishizuka N, <u>Saijo N.</u>	Standard thoracic radiotherapy with or without concurrent daily low-dose carboplatin in elderly patients with locally advanced non-small cell lung cancer: a phase III trial of the Japan Clinical Oncology Group (JCOG9812).	Jpn J Clin Oncol	35(4)	195-201	2005
<u>Saijo N.</u> , Nimura Y.	Summary of the ASCO-JSCO joint symposium.	Int J Clin Oncol	10(3)	153-156	2005
Shimizu K, Yamada K, Saito H, <u>Noda K.</u> , Nakayama H, Kameda Y, Nakata K.	Surgically curable peripheral lung carcinoma Correlation of thin-section CT findings with histologic prognostic factors and survival.	Chest	127(3)	871-878	2005
Nishio K, Arai T, Shimoyama T, Fujiwara Y, Tamura T, <u>Saijo N.</u>	Translational studies for target-based drugs.	Cancer Chemother Pharmacol	56(Suppl 7)	90-93	2005

Masahiro Endo, Hiroyoshi Furukawa, Takeshi Aramaki, Naoki Morimoto, Takayoshi Uematsu, Seigo Yukisawa, Sachiko Yuen, Nobuyuki Yamamoto, Yasuhisa Ohde, Haruhiuko Kondo, Koji Amano	Unusual late pulmonary complication in a child after umbilical cord blood transplantation High-resolution CT – pathologic correlation	J Thoracic Imaging	20	103-106	2005
Saijo N.	What phase III trials are needed to improve the treatment of advanced non-small-cell lung cancer?	Nat Clin Pract Oncol	2(6)	275	2005
大江裕一郎	わが国の大規模臨床試験FACSの成績から.	呼吸器 NEWS&VIEWS	27		2005
中野絵里子、加藤晃史、大江裕一郎	進行非小細胞肺癌の化学療法.	MOOK2004-2005 肺癌の臨床		237-245	2005
Kudoh S, Takeda K, Nakagawa K, Takada M, Katakami N, Matsui K, Shinkai T, Sawa T, Goto I, Semba H, Seto T, Ando M, Satoh T, Yoshimura N, Negoro S, Fukuoka M	Phase III Study of Docetaxel Compared With Vinorelbine in Elderly Patients With Advanced Non-Small-Cell Lung Cancer: Results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904)	Journal of Clinical Oncology	24(22)	3657-3663	2006
Kawahara M	Irinotecan in the treatment of small cell lung cancer: a review of patient safety considerations	Expert Opin Drug Saf	5	303-312	2006
Ando M, Okamoto I, Yamamoto N, Takeda K, Tamura K, Seto T, Ariyoshi Y, Fukuoka M	Predictive Factors for Interstitial Lung Disease, Antitumor Response, and Survival in Non-Small-Cell Lung Cancer Patients Treated With Gefitinib	Journal of Clinical Oncology	24(16)	2549-2556	2006
Okamoto H, Naoki K, Narita Y, Hida N, Kunikane H, Watanabe K.	A combination chemotherapy of carboplatin and irinotecan with granulocyte colony-stimulating factor (G-CSF) support in elderly patients with small cell lung cancer.	Lung Cancer	53	197-203	2006
Sekine I, Minna JD, Nishio K, Tamura T, Saijo N.	A literature review of molecular markers predictive of clinical response to cytotoxic chemotherapy in patients with lung cancer.	J Thorac Oncol	1(1)	31-37	2006
Tamura T, Minami H, Yamada Y, Yamamoto N, Shimoyama T, Murakami H, Horiike A, Fujisaka Y, Shinkai T, Tahara M, Kawada K, Ebi H, Sasaki Y, Jiang H, Saijo N.	A phase I dose-escalation study of ZD6474 in Japanese patients with solid, malignant tumors.	J Thoracic Oncol	1(9)	1002-1009	2006
Kaneda, H., Kurata, T., Tamura, K., Uejima, H., Nakagawa, K., Fukuoka, M.	A Phase I Study of Irinotecan in Combination with Amrubicin for Advanced Lung Cancer Patients.	Anticancer Res.	26	2479-2486	2006
Nakagawa K., Kudoh S., Matsui K., Negoro S., Yamamoto N., Latz J. E., Adachi S., Fukuoka M.	A phase I study of pemetrexed (LY231514) supplemented with folate and vitamin B12 in Japanese patients with solid tumours.	Br. J. Cancer	95	677-682	2006
Hyodo, I., Shirao, K., Doi, T., Hatake, K., Arai, Y., Yamaguchi, K., Tamura, T., Takemiya, S., Takiuchi, H., Nakagawa, K., Mishima, H.	A phase II Study of the global dose and schedule of capecitabine in Japanese patients with metastatic colorectal cancer.	Jpn J Clin Oncol	36	410-417	2006
Yatabe Y, Hida T, Horio Y, Kosaka T, Takahashi T, Mitsudomi T.	A rapid, sensitive assay to detect EGFR mutation in small biopsy specimens from lung cancer.	J Mol Diagn.	8	335-41	2006
Kawahara K, Nagano T, Inoue T, Tada H, Okamoto N, Sasada S, Kobayashi M, Matsui K.	An extremely solid variant of adenoid cystic carcinoma arising in the lower tracheas.	Arch Histopathol	13	10_14	2006
Kosaka T, Yatabe Y, Endoh H, Yoshida K, Hida T, Tsuboi M, Tada H, Kuwano H, Mitsudomi T.	Analysis of epidermal growth factor receptor gene mutation in patients with non-small cell lung cancer and acquired resistance to gefitinib.	Clin Cancer Res.	12	5764-69	2006

Suzuki M, <u>Nishimura Y</u> , Nakamatsu K, Okumura M, Hashiba H, Koike R, Kanamori S, Shibata T.	Analysis of interfractional set-up errors and intrafractional organ motions during IMRT for head and neck tumors to define an appropriate planning target volume (PTV)- and planning organs at risk volume (PRV)-margins.	Radiotherapy and Oncol.	78	283-90	2006
Sasada S, Ogata Y, Kobayashi M., Hirashima T., Kawahara K., <u>Matsui K</u> , Kawase I.	Angled forceps used for transbronchial biopsy in which standard forceps are difficult to manipulate; a comparative study.	Chest	29(3)	725-723	2006
Watanabe Y, LePage S, Elliott M, Secrist H, Tanaka T, <u>Kawahara M</u> , Matsumura A, Hosoe S, Ogawara M, Okada M, Repasky B, Sleath P, Wang T, Henderson R	Characterization of preexisting humoral immunity specific for two cancer-testis antigens overexpressed at the mRNA level in non-small cell lung cancer.	Cancer Immun	6		2006
<u>Nakagawa K</u> .	Clinical development of EGFR-tyrosine kinase inhibitors in Japan.	Cancer Chemother Pharmacol	58	33-37	2006
Sekine I, Nokihara H, <u>Yamamoto N</u> , Kunitoh H, Ohe Y, <u>Saijo N</u> , Tamura T.	Common arm analysis: one approach to develop the basis for global standardization in clinical trials of non-small cell lung cancer.	Lung cancer	53(2)	157-164	2006
Tomiyama N, Yasuhara Y, Nakajima Y, Adachi S, Arai Y, Kusumoto M, Eguchi K, Kuriyama K, Sakai F, Noguchi M, Murata K, Murayama S, Mochizuki T, <u>Mori K</u> , Yamada K	CT-guided needle biopsy of lung lesions: A survey of severe complication based on 9783 biopsies in Japan	Eur J Radiology	59	60-64	2006
Nomoto K, Tsuta K, Takano T, Fukui T, Fukui T, Yokozawa K, Sakamoto H, Yoshida T, Maeshima AM, Shibata T, Furuta K, <u>Ohe Y</u> , Matsuno Y	Detection of EGFR Mutations in Archived Cytologic Specimens of Non-Small Cell Lung Cancer Using High-Resolution Melting Analysis	Am J Clin Pathol	126	608-615	2006
Sakai K, Arai T, Shimoyama T, Murofushi K, Sekijima M, Kaji N, Tamura T, <u>Saijo N</u> , Nishio K.	Dimerization and the signal transduction pathway of a small in-frame deletion in the epidermal growth factor receptor.	FASEB J	20(2)	311-313	2006
Sekine I, Nokihara H, Sumi M, <u>Saijo N</u> , Nishiwaki Y, Ishikura S, Mori K, Tsukiyama I, Tamura T.	Docetaxel consolidation therapy following cisplatin, vinorelbine, and concurrent thoracic radiotherapy in patients with unresectable stage III non-small cell lung cancer.	J Thoracic Oncol	1(8)	810-815	2006
Ohira T, Suga Y, <u>Kato H</u> , et al.	Early-stage lung cancer: diagnosis and treatment	Int J Clin Oncol	11(1)	9-12	2006
Hitoshi Ishikawa, Yuko Nakayama, Yoshizumi Kitamoto, Tetsuo Nonaka, Hidemasa Kawamura, Katsuyuki Shirai, Hideyuki Sakurai, <u>Kazushige Hayakawa</u> , Hideo Niibe, Takashi Nakano	Effect of histologic type on recurrence pattern in radiation therapy for medically inoperable patients with stage I non-small-cell lung cancer	Lung	184	347-353	2006
Watanabe H, Kunitoh H, Yamamoto S, Kawasaki S, Inoue A, Hotta K, Shiomi K, Kusumoto M, Sugimura K, <u>Saijo N</u> .	Effect of the introduction of minimum lesion size on interobserver reproducibility using RECIST guidelines in non-small cell lung cancer patients.	Cancer Sci	97(3)	214-218	2006
Shimoyama T, Koizumi F, Fukumoto H, Kiura K, Tanimoto M, <u>Saijo N</u> , Nishio K.	Effects of different combinations of gefitinib and irinotecan in lung cancer cell lines expressing wild or deletional EGFR.	Lung Cancer	53(1)	13-21	2006
Saijo T.	Eg5 expression is closely correlated with the response of advanced non-small cell lung cancer to antimitotic agents combined with platinum chemotherapy	Lung Cancer	Volume 54(2)	135-266	2006
Sasaki H., Shimizu S., Endo K., Takada M., <u>Kawahara M</u> , Tanaka H., Matsumura A., Iuchi K., Haneda H., Suzuki E., Kobayashi Y., Yano M. and Fujii Y.	EGFR and ErbB2 mutation status in Japanese lung cancer patients	Int J Cancer	118	180-184	2006

Okamoto, I., Araki, J., Suto, R., Shimada, M., <u>Nakagawa, K.</u> , <u>Fukuoka M.</u>	EGFR mutation in gefitinib-responsive small-cell lung cancer.	Ann Oncol.	17	1028-1029	2006
Yoshimura N, Kudoh S, Kimura T, Mitsuoka S, Matsuura K, Hirata K, <u>Matsui K</u> , <u>Negoro S</u> , <u>Nakagawa K</u> , and <u>Fukuoka M</u> .	EKB-569, a new irreversible epidermal growth factor receptor tyrosine kinase inhibitor, with clinical activity in patients with non-small cell lung cancer with acquired resistance to gefitinib.	Lung Cancer	51	363-368	2006
Usami N, Fukui T, Kondo M, Taniguchi T, Yokoyama T, Mori S, Yokoi K, Horio Y, Shimokata K, Sekido Y, <u>Hida T</u> .	Establishment and characterization of four malignant pleural mesothelioma cell lines from Japanese patients.	Cancer Sci.	97	387-94	2006
Niho S, Kubota K, Goto K, Yoh K, Ohmatsu H, Kakinuma R, <u>Saijo N</u> , <u>Nishiwaki Y</u> .	First-line single agent treatment with gefitinib in patients with advanced non-small-cell lung cancer: a phase II study.	J Clin Oncol	24(1)	64-69	2006
Yoshimura M, <u>Imamura F</u> , Ueno K, Uchida J.	Gemcitabine/carboplatin in a modified 21-day administration schedule for advanced-stage non-small-cell lung cancer.	Clin Lung Cancer	8(3)	208-13	2006
Oshita F, Sekiyama A, Saito H, Yamada K, <u>Noda K</u> , Miyagi Y.	Genome-wide cDNA microarray screening of genes related to the benefits of paclitaxel and irinotecan chemotherapy inpatients with advanced no-small cell lung cancer.	J Exp Ther Onc	6	49-53	2006
Edelman MJ, Sekine I, Tamura T, <u>Saijo N</u> .	Geographic variation in the second-line treatment of non-small cell lung cancer.	Semin Oncol	33(1 Suppl 1)	S39-44	2006
Saeki M, Saito Y, Jinno H, Sai K, Ozawa S, Kurose K, Kaniwa N, Komamura K, Kotake T, Morishita H, Kamakura S, Kitakaze M, Tomoike H, Shirao K, Tamura T, <u>Yamamoto N</u> , Kunitoh H, Hamaguchi T, Yoshida T, Kubota K, Ohtsu A, Muto M, Minami H, <u>Saijo N</u> , Kamatani N, Sawada JI.	Haplotype structures of the UGT1A gene complex in a Japanese population.	Pharmacogenomics J	6(1)	63-75	2006
<u>Imamura F</u> , Ueno K, Kusunoki Y, Uchida J, Yoshimura M, Koizumi M, Yamasaki H, Nishiyama K.	High-dose-rate brachytherapy for small-sized peripherally located lung cancer.	Strahlenther Onkol.	182(12)	703-7	2006
<u>原田英博</u> , <u>新明裕子</u> , <u>大江裕一郎</u>	Ⅲ期非小細胞肺がんの放射線化学療法	呼吸器科	9	93-100	2006
Masahiro Endo, Takeshi Johkoh, Kazuhiko Kimura, <u>Nobuyuki Yamamoto</u>	Imaging of gefitinib-related interstitial lung disease: multi-institutional analysis of West Japan Thoracic Oncology Group	Lung Cancer	52	135-140	2006
Sakai K, Yokote H, Murakami-Murofushi K, Tamura T, <u>Saijo N</u> , Nishio K.	In-frame deletion in the EGF receptor alters kinase inhibition by gefitinib.	Biochem J	397(3)	537-543	2006
Niho S, Goto K, Yoh K, Kim Y, Ohmatsu H, Kubota K, <u>Saijo N</u> , <u>Nishiwaki Y</u> .	Interstitial shadow on chest CT is associated with the onset of interstitial lung disease caused by chemotherapeutic drugs.	Jpn J Clin Oncol	36	269-273	2006
Uchida J, <u>Imamura F</u> , Takenaka A, Yoshimura M, Ueno K, Oda K, Nakayama T, Tsukamoto Y, Higashiyama M, Kusunoki Y.	Improved diagnostic efficacy by rapid cytology test in fluoroscopy-guided bronchoscopy.	J Thorac Oncol	1(4)	314-8	2006